EXHIBIT A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Michael Wayne Graham et al.	
Serial No.:	09/100,812	Examiner: Sumesh Kaushal
Filed:	19 June 1998	Art Unit: 1633
For:	Synthetic genes and genetic constructs comprising same I	Docket: 11535

Commissioner of Patents and Trademarks
Washington D.C. 20231

SUPPLEMENTAL DECLARATION OF MICHAEL WAYNE GRAHAM

Sir,

I, Michael Wayne Graham, state as follows:

My present position is Principal Research Scientist of Benitec Australia Ltd, one of the assignees of the subject application (serial no. 09/100,812). I am one of the co-inventors named in the above-identified application. I have also made a declaration in support of this application on 23 April 2002 (which I refer to as my 'Earlier Declaration'). My Earlier Declaration contains evidence of my background and experience. I provide further detail of the particular constructs mentioned in my Earlier Declaration as follows.

In each of the two constructs pCMV.BEV2.GFP.2VEB and pCMV.BEV2.BGI2.2VEB, the structural gene sequence comprised a nucleotide sequence present in the sense and antisense orientations having 1,387 bp. This sequence corresponded to the region spanned by nucleotides 5,951 to 7,337 of the BEV virion, which is itself 7,405 nt long. The nucleotide sequence further included at its 5' end the 9 extra bases AACAATGGC, and at its 3' end the 9 extra bases GCCATTGTT, neither of which are present in the target gene.

The structural gene sequence of each of the two constructs pCMV.TYR.BGI2.RYT and pCMV.TYR.TYR had a nucleotide sequence of 1,429 bp. It was taken from the region spanning nucleotides 203 to 1,772 of the cDNA sequence of 3,408 bp (derived from the mRNA transcription product of the target gene) but for a 148 bp deletion at position 1,199 of the reference cDNA sequence and a 7 bp insertion at position 1,355 of the reference cDNA sequence. Accordingly, on a simple percentage homology

analysis, the structural gene sequence of this particular example is about 90% identical to the target gene region.

The structural gene sequence of the construct pCMV.HER2.BGI2.2REH contained a 917 bp nucleotide sequence, obtained from nucleotides 221 to 1,137 of the cDNA sequence of 4,530 bp, which was derived from the mRNA transcription product of the target gene.

The structural gene sequence of the construct pCMV.YB1.BGI2.1BY contained a 963 bp nucleotide sequence, obtained from nucleotides 526 to 1,488 of the reference cDNA sequence of 1,512 bp, which was derived from the mRNA transcription product of the target gene. An additional (extraneous) 4 bp was inserted into the nucleotide sequence by cutting and end-filling an *Afl*II site at position 1,197 of the reference sequence.

The structural gene sequence of the construct pCMV.YB1.p53.BGI2.35p.1BY comprised a nucleotide sequence being the 963 bp nucleotide sequence of the construct pCMV.YB1.BGI2.1BY mentioned immediately above, collinear with the 1,067 bp nucleotide sequence obtained from nucleotides 631 to 1,697 of the reference p53 cDNA sequence of 2,149 bp, which was derived from the mRNA transcription product of the target gene. Thus, about half of the nucleotide sequence (in both the sense and antisense orientations) was dissimilar to each of the targeted genes YB1 and p53 in that the nucleotide sequence used to target YB1 included 1,067 bp of 3' unrelated (p53) sequence and the nucleotide sequence used to target p53 included 963 bp of 5' unrelated (YB1) sequence.

I also clarify the results of the experiment using this construct, in addition to my comments at lines 17 to 29 of page 11 of my Earlier Declaration. The assay for the YB1 construct (shown in Annexure MWG9) was cell death (apoptosis), as described; the assay for the combined YB1.p53 construct (shown in Annexure MWG10) was again cell death (apoptosis), but the efficacy of this latter construct was determined from the *decrease* (not increase) in cell death compared with the YB1 construct alone, i.e. reduction in apoptosis resulting from downregulation of p53, whose endogenous levels were increased by release of YB1 repression resulting from YB1 downregulation.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge and wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such wilful false statements may jeopardise the validity of the application or any patent issuing thereon.

Date 23/9/02 By _____

Michael Wayne Graham